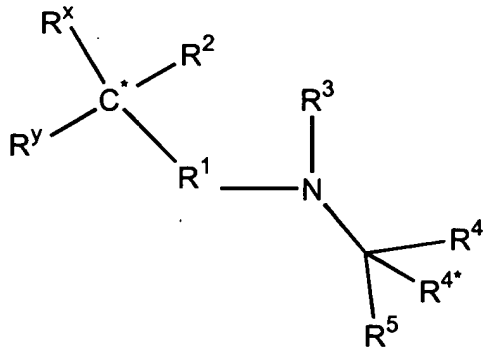
APPENDIX A2: CHANGES TO CLAIMS (VERSION WITH MARKINGS TO SHOW CHANGES MADE, I.E., REDLINE)

43. **(Amended)** A compound of the following formula:



or a pharmaceutically acceptable salt thereof,

wherein:

(1) C^* is a substituted carbon;

(2) R^2 (a) is hydrogen, (C1-C6) alkyl, (C1-C6) alkoxy, cyano, (C2-C7) alkanoyl, aminocarbonyl, (C1-C6) alkylaminocarbonyl, or dialkylaminocarbonyl wherein each alkyl is independently C1 to C6, (b) comprises (where R^1 is not aminoethylene, -O-R^8 or -S-R^{8*}) hydroxy, fluoro, chloro, bromo or (C2-C7) alkanoyloxy, (c) forms a double bond with an adjacent carbon or nitrogen from one of either R^1, R^{xb} or R^{yb}, (d) is R^{2a} linked by R^{2b} to C*, or (e) is ethylene forming a third bridging structure as set forth in (2^{iii})(c)(i) ~~(2^{iii})(b)(i)~~;

(2^i) R^x is R^{xa} linked by R^{xb} to C^*;

(2^{ii}) R^y is R^{ya} linked by R^{yb} to C^*;

(2^{iii}) R^{xa} and R^{ya}, are independently Ar, which is phenyl or naphthyl, heteroaryl, or or a 5 to 7-membered non-aromatic ring having from 0 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, and R^{2a}, when present, is Ar, and wherein:

(a) heteroaryl comprises thienyl, furanyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, or one of the foregoing fused to phenyl, or methylenedioxyphenyl,

APPENDIX A2: CHANGES TO CLAIMS (REDLINE) – (continued)

(b) each of R^{xa} and R^{ya} can be independently substituted with one of R^q, R^rO- or R^sS-, wherein each of R^q, R^r and R^s are independently Ar, heteroaryl, adamantyl, or a 5 to 7-membered non-aromatic ring having from 0 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, and

(c) R^{xa}, R^{ya}, R^{2a}, R^q, R^r and R^s can be substituted or additionally substituted with one or more substituents selected from the group consisting of fluoro, chloro, bromo, nitro, hydroxy, cyano, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, (C1-C12) alkyl, (C2-C12) alkenyl, amino, (C1-C6) alkylamino, dialkylamino wherein each alkyl of dialkylamino is independently C1 to C6, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be substituted for hydrogen with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, or amidino wherein the amidino can be independently substituted with up to three (C1-C6) alkyl groups, wherein:

(i.) the substitutions of R^{xa} and R^{ya} can be combined to form a second bridge between R^{xa} and R^{ya} comprising (1) methylene or ethylene, which methylene or ethylene can be substituted by ~~an~~ R^2 when R^2 is ethylene to form the third bridging structure, or (2) -CH=CH-, or (3) sulfur, or (4) oxygen, or wherein R^{xa} and R^{ya} can be directly linked by a single bond,

(d) wherein at least one of R^{xa}, R^{ya}, R^q, R^r or R^s is heteroaryl, or a second bridge between R^{xa} and R^{ya} comprises sulfur or oxygen as set forth below, or Ar substituted with a methylenedioxy;

(2^{iv}) R^{xb} and R^{2b} are independently a single bond or (C1-C2) alkylene;

APPENDIX A2: CHANGES TO CLAIMS (REDLINE) – (continued)

(2^{v}) R^{yb} is a single bond, oxy, (C1-C2) alkylene, ethenylene or -CH= (where the double bond is with C^{*}), thio, methyleneoxy or methylenethio, or either -N(R^{6}) or -CH_2-N(R^{6*})-, wherein R^{6} and R^{6*} are hydrogen or (C1-C6) alkyl;

(3) R^{1} comprises: a straight-chained (C2-C3) aliphatic group; =N-O-(ethylene), wherein the unmatched double bond is linked to C^{*}; -O-R^{8} or -S-R^{8*} wherein R^{8} or R^{8*} is a ethylene or ethenylene and O or S is bonded to C^{*}; aminoethylene where the amino is bonded to C^{*}:

wherein R^{1} can be substituted with up to one hydroxy, up to one (C1-C6) alkoxy or up to one (C2-C7) alkanoyloxy, with up to two independent (C1-C6) alkyl, with up to one oxo, up to one (C1-C6) alkylidene, with the proviso that the hydroxy, alkoxy, alkanoyloxy or oxo substituents are not bonded to a carbon that is bonded to a nitrogen or oxygen;

wherein if R^{1} contributes a heteroatom linked to C^{*}, then R^{yb} does not contribute a heteroatom linked to C^{*}; and

wherein the alkyl or alkylidene substituents of R^{1} can be linked to form a 3 to 7-membered non-aromatic ring;

(4) R^{3} (a) is hydrogen, (C1-C6) alkyl, or phenyl or phenylalkyl wherein the alkyl is C1 to C6 and the phenyl or phenyl of phenylalkyl can be substituted with the same substituents defined above for the phenyl of R^{xa}, (b) is -R^{12}C(R^{xx})(R^{yy})(R^{11}), wherein R^{12} is bonded to N , R^{xx} is independently the same as R^{x}, R^{yy} is independently the same as R^{y}, R^{11} is independently the same as R^{2} and R^{12} is independently the same as R^{1};

(5) R^{4} and R^{4*} are independently hydrogen or (C1-C6) alkyl, or one of R^{4} and R^{4*} can be (C1-C6) hydroxyalkyl; and

APPENDIX A2: CHANGES TO CLAIMS (REDLINE) – (continued)

(6) R^5 is $(CO)NR^{13}R^{14}$, $(CO)OR^{15}$, $(CO)SR^{16}$, $(SO_2)NR^{17}R^{18}$, $(PO)(OR^{19})(OR^{20})$, $(CR^{22})(OR^{23})(OR^{24})$, CN or tetrazol-5-yl, wherein (a) R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18} R^{19} and R^{20} are independently hydrogen, (C1-C8) alkyl which can include a (C3-C8) cycloalkyl, wherein the carbon linked to the oxygen of R^{15} or the sulfur of R^{16} has no more than secondary branching, (C2-C6) hydroxyalkyl, aminoalkyl where the alkyl is C2 to C6 and the amino can be substituted with up to two independent (C1-C6) alkyls, Ar-alkyl wherein the alkyl is C1-C6, or Ar, and (b) R^{22} is hydrogen or OR^{25} and R^{23} , R^{24} and R^{25} are independently (C1-C6) alkyl, phenyl, benzyl or acetyl or, the alkyls of R^{23} and R^{24} can be combined to include 1,3-dioxolane or 1,3-dioxane:

wherein the phenyl or naphthyl groups of R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{22}, R^{23} or R^{24} can be substituted with substituents selected from the group consisting of fluoro, chloro, bromo, nitro, cyano, hydroxy, trifluoromethyl, amidosulfonyl which can have up to two independent (C1-C6) N-alkyl substitutions, (C1-C6) alkyl, (C2-C6) alkenyl, (C1-C6) alkylamine, dialkylamine wherein each alkyl is independently C1 to C6, amino, (C1-C6) alkoxy, (C2-C7) alkanoyl, (C2-C7) alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be N-substituted with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, or amidino that can <u>be</u> substituted with up to three (C1-C6) alkyl;

wherein R^{13} and R^{14} together with the attached nitrogen can form a 5 to 7-membered ring.

46. **(Amended)** The compound of claim 43, wherein (A) at least one of R^{xa}, R^{ya} and R^{2a} is substituted with fluoro, chloro, bromo, hydroxy, trifluoromethyl, trifluoromethoxy, nitro, cyano

APPENDIX A2: CHANGES TO CLAIMS (REDLINE) – (continued)

alkanoyloxy, trifluoromethoxy, hydroxycarbonyl, (C2-C7) alkyloxycarbonyl, aminocarbonyl that can be N-substituted with up to two independent (C1-C6) alkyl, (C1-C6) alkylsulfonyl, amidino that can substituted with up to three (C1-C6) alkyl.

APPENDIX B1: REPLACEMENT PARAGRAPHS (CLEAN COPY)

Change 1- Please amend the first paragraph at page 1, lines 4-7 as follows:

C6 The present application is a divisional application of U.S. Serial No. 08/866,007, filed May 30, 1997, now U.S. Patent No. 6,191,165 which claims the benefit of priority of: U.S. Serial No. 60/041,503, filed May 31, 1996, U.S. Serial No. 60/041,504, filed May 31, 1996, U.S. Serial No. 60/070,900, filed February 27, 1997 and U.S. Serial No. 60/044,387, filed February 27, 1997.

APPENDIX B2: REPLACEMENT PARAGRAPHS (VERSION WITH MARKINGS TO SHOW CHANGES MADE, I.E., REDLINE)

Change 1- Please amend the first paragraph at page 1, lines 4-7 as follows:

The present application is a divisional application of U.S. Serial No. 08/866,007, filed May 30, 1997, now U.S. Patent No. 6,191,165 which claims the benefit of priority ~~is a continuation-in-part~~ of: U.S. Serial No. 60/041,503, ~~08/656,063,~~ filed May 31, 1996, U.S. Serial No. 60/041,504, ~~08/655,912~~ filed May 31, 1996, U.S. Serial No. 60/070,900, ~~08/807,682~~ filed February 27, 1997 and U.S. Serial No. 60/044,387, ~~08/808,754,~~ filed February 27, 1997~~, each of which applications are now converted to provisional applications~~.